

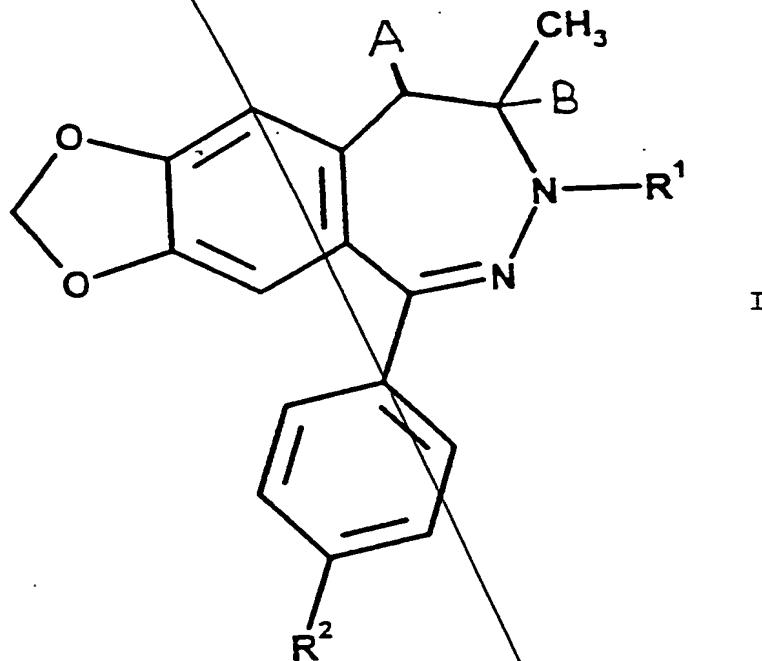
-102-

Claims:

1. A 1,3-dioxolo/4,5-h//2,3/benzodiazepine derivative of the formula I

Deck

B'



wherein

A represents a hydrogen atom,

B means a hydrogen atom,

 R^1 stands for a group of the formula $-(CH_2)_n-CO-(CH_2)_m-R$, whereinR represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein R^3 and R^4 mean, independently, a hydrogenatom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group,

a phenyl group optionally substituted

by one or two C_{1-4} alkyl group(s),a C_{1-4} alkyl group which latter is

-103-

B1
Cont

000760-000760

optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula $-CO-(CH_2)_p-R^6$, wherein

R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

-104-

B /
Cont

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxyl group, or R^7 and R^8 form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group which latter is optionally substituted, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is

05435441.064000

-105-

B1
Cont

optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C₁₋₄ alkoxy group, and, in case of the phenoxy(C₁₋₄ alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,
R² stands for a nitro group, an amino group or a (C₁₋₄ alkanoyl)amino group, and pharmaceutically suitable acid addition salts thereof.

2. A 1,3-dioxolo[4,5-h]2,3/benzodiazepine derivative as claimed in Claim 1, wherein A represents a hydrogen atom, B means a hydrogen atom, R¹ stands for a group of the formula -(CH₂)_n-CO-(CH₂)_m-R, wherein R represents a chloro atom, a pyridyl group or a group of the formula -NR³R⁴, wherein R³ and R⁴ mean, independently, a hydrogen atom, a cyclopropyl group, a C₁₋₄ alkoxy group, an amino group, a phenyl group optionally substituted by one or two methyl group(s) or a C₁₋₄ alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom

00076-05-000

-106-

B1
Cont

as the heteroatom, and the heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 methoxy groups,

or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 methoxy groups, n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2,

R^2 stands for a nitro group or an amino group, and pharmaceutically suitable acid addition salts thereof.

3. A 1,3-dioxolo/4,5-h/2,3/benzodiazepine derivative as claimed in Claim 2, wherein R^3 and R^4 represent, independently, a hydrogen atom, a cyclopropyl group, a methoxy group, an amino group, a dimethylaminophenyl group or a C_{1-2} alkyl group which latter is substituted by a phenyl, morpholino or piperazinyl group, wherein the piperazinyl group is substituted by a methoxyphenyl group, or

R^3 and R^4 form, together with the adjacent nitrogen atom and optionally a further nitrogen atom or oxygen atom, an imidazolyl, morpholino or piperazinyl group, wherein

SEARCHED - SERIALIZED - INDEXED - FILED

-107-

B1
Cont

the piperazinyl group is substituted by a methoxyphenyl group,
n has a value of 0 or 1,
m has a value of 0 or 1,
 R^2 stands for a nitro group or an amino group,
A represents a hydrogen atom,
B means a hydrogen atom,
and pharmaceutically suitable acid addition salts thereof.

4. A 1,3-dioxolo[4,5-h][2,3/benzodiazepine derivative as claimed in Claim 3, wherein
 R^3 represents a hydrogen atom,
 R^4 stands for a cyclopropyl group, a methoxy group or an amino group,
n has a value of 0,
m has a value of 0,
 R^2 means an amino group,
A represents a hydrogen atom,
B means a hydrogen atom,
and pharmaceutically suitable acid addition salts thereof.

5. A 8-methyl-7H-1,3-dioxolo[4,5-h][2,3/benzodiazepine derivative as claimed in Claim 1, wherein in formula I
A forms together with B a valence bond between the carbon atoms in positions 8 and 9,
 R^1 represents a group of the formula $-\text{CO}-(\text{CH}_2)_p-\text{R}^6$, wherein
 R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-\text{NR}^7\text{R}^8$, wherein

CONFIDENTIAL

-108-

*BT
cont*

DEPARTMENT OF DOCUMENTS

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a morpholino group, wherein the phenyl group is optionally substituted by one or two C_{1-2} alkoxy group(s), or

R^7 and R^8 form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group or a saturated heterocyclic group having 5 or 6 members and comprising one or two nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 2 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by a halo atom or a C_{1-4} alkoxy group,

p has a value of 0, 1 or 2,

R^2 stands for a nitro group or an amino group, and pharmaceutically suitable acid addition salts thereof.

6.. A 8-methyl-7H-1,3-dioxolo[4,5-h]//2,3/-

-109-

B1
Cont

benzodiazepine derivative as claimed in Claim 5, wherein

A forms together with B a valence bond between the carbon atoms in positions 8 and 9,

R² represents a nitro group or an amino group,

R¹ stands for a group of the formula

$-\text{CO}-(\text{CH}_2)_p-\text{R}^6$, wherein

R⁶ means a chloro atom, a phenoxy group, or a group of the formula -NR⁷R⁸, wherein

R⁷ and R⁸ represent, independently, a hydrogen atom, a guanyl group or a C₁₋₃ alkyl group optionally substituted by a phenyl group, a dimethoxyphenyl group or a morpholino group, or

R⁷ and R⁸ form with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group or a saturated heterocyclic group having 5 or 6 members and comprising one or two nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by one or two identical or different substituent(s) selected from the group consisting of a hydroxy group, a methoxyphenyl group, a fluorophenyl group, a benzyl group or a (methoxyphenoxy)-(hydroxypropyl) group,

p has a value of 0, 1 or 2,

-110-

and pharmaceutically suitable acid addition salts thereof.

B1
cont

7. A 8-methyl-7H-1,3-dioxolo[4,5-h]2,3-benzodiazepine derivative as claimed in Claim 6, wherein

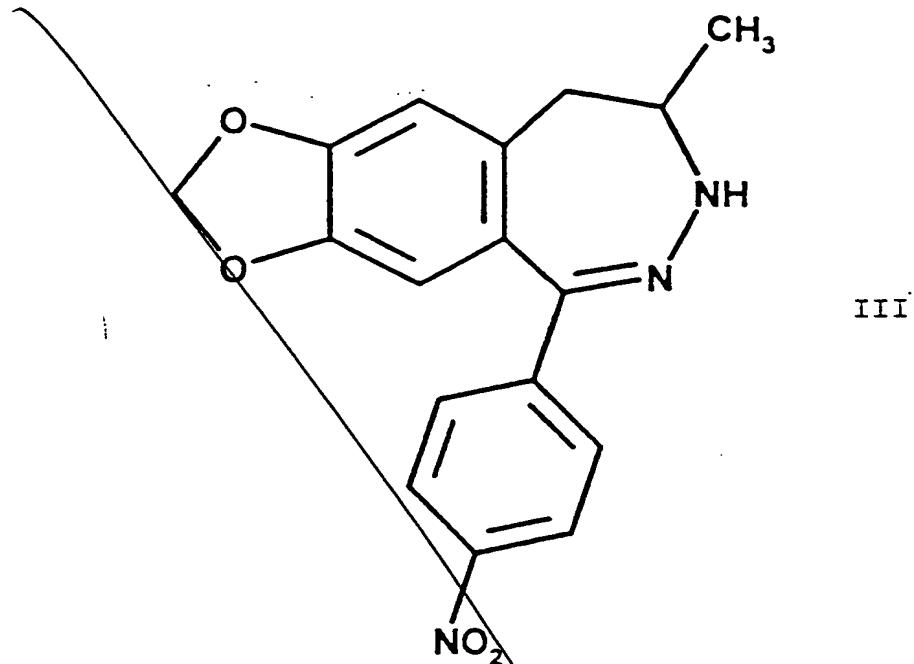
R^2 represents an amino group,
 R^1 , A and B are as defined in Claim 6, and pharmaceutically suitable acid addition salts thereof.

8. A process for the preparation of a 1,3-dioxolo[4,5-h]2,3-benzodiazepine derivative of the formula I, wherein R^1 and R^2 are as defined in Claim 1, and pharmaceutically suitable acid addition salts thereof, characterized in that

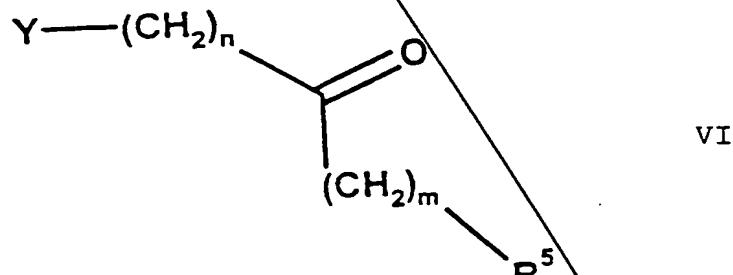
a) for the preparation of a compound of the formula I, wherein R^1 represents a group of the formula $-(CH_2)_n-CO-(CH_2)_m-R$, wherein R stands for a halo atom or a pyridyl group, n has a value of 0, 1 or 2, m has a value of 0, 1 or 2, R^2 means a nitro group, A and B represent a hydrogen atom, the 7,8-dihydro-8-methyl-5-(4-nitrophenyl)-9H-1,3-dioxolo[4,5-h]2,3-benzodiazepine of the formula III

CONFIDENTIAL

-111-

B1
Cont

is reacted with a reagent of the formula VI



wherein Y represents a leaving group, R⁵ is a halo atom or a pyridyl group; or

b) for the preparation of a compound of the formula I, wherein R¹ represents a group of the formula -(CH₂)_n-CO-(CH₂)_m-R, wherein R stands for an imidazolyl group, n has a value of 0, m has a value of 0, R² means a nitro group, A and B represent a

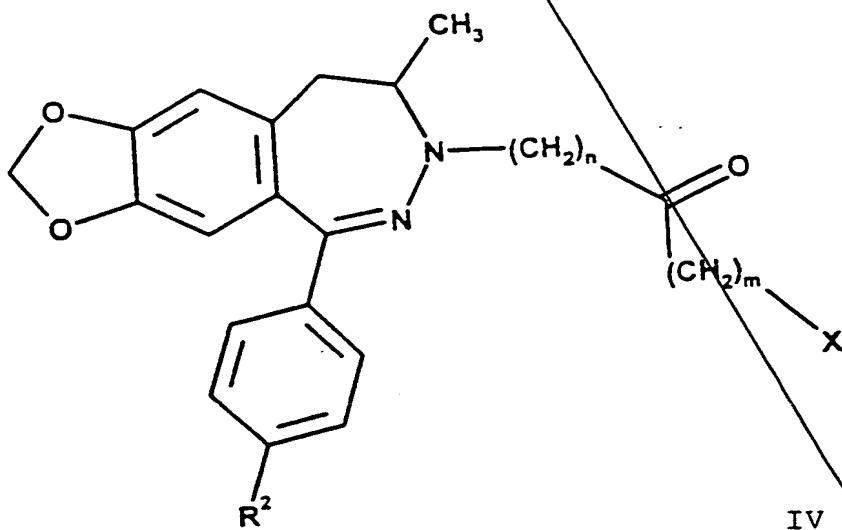
-112-

B1
Cont

DOCUMENT - PCT/HU98/00076

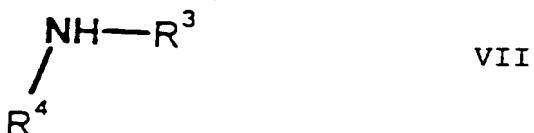
hydrogen atom, the 7,8-dihydro-8-methyl-5-(4-nitrophenyl)-9H-1,3-dioxolo[4,5-h]2,3/benzodiazepine of the formula III is reacted with 1,1'-carbonyldiimidazole; or

c) for the preparation of a compound of the formula I, wherein R^1 represents a group of the formula $-(CH_2)_n-CO-(CH_2)_m-R$, wherein R stands for a group of the formula $-NR^3R^4$, wherein R^3 , R^4 , n and m are as defined in connection with formula I, R^2 means a nitro group, A and B represent a hydrogen atom, the 7,8-dihydro-8-methyl-5-(4-nitrophenyl)-9H-1,3-dioxolo[4,5-h]2,3/benzodiazepine of the formula III is reacted with a reagent of the formula VI, wherein Y and R^5 represent, independently, a leaving group, n and m are as stated above, and the obtained benzodiazepine derivative of the formula IV

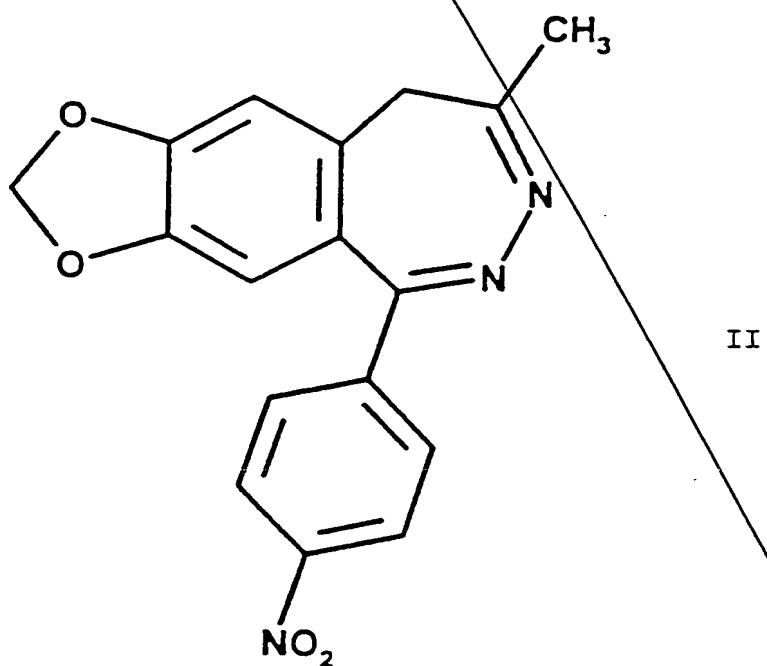


-113-

wherein X stands for a leaving group, n and m are as stated above, is reacted with an amine of the formula VII



wherein R^3 and R^4 are as stated above; or
 d) for the preparation of a compound of the formula I, wherein R^1 stands for a group of the formula $-\text{CO}-(\text{CH}_2)_p-\text{R}^6$, wherein R^6 represents a halo atom, a phenoxy group or a C_{1-4} alkoxy group, p has a value of 0, 1 or 2, A forms together with B a valence bond, R^2 means a nitro group, the 8-methyl-5-(4-nitrophenyl)-9H-1,3-dioxolo[4,5-h]2,3-benzodiazepine of the formula II



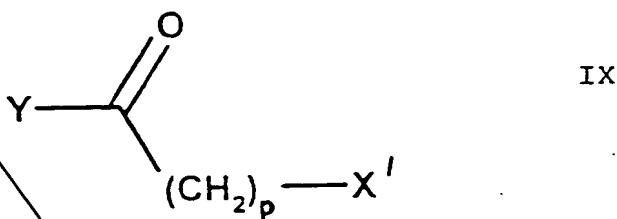
DELEGATEN-054000

B1
cont

-114-

B1
Cont

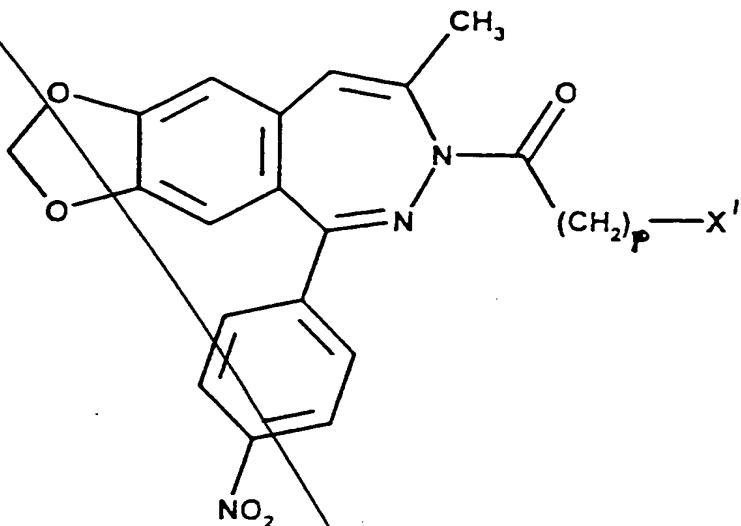
is reacted with an acylating agent of the formula IX



wherein Y represents a leaving group, X' stands for a halo atom, a phenoxy group or a C_{1-4} alkoxy group, p has a value of 0, 1 or 2; or

e) for the preparation of a compound of the formula I, wherein R^1 stands for a group of the formula $-CO-(CH_2)_p-R^6$, wherein R^6 represents a group of the formula $-NR^7R^8$, wherein R^7 , R^8 and p are as defined in connection with the formula I. A forms together with B a valence bond, R^2 means a nitro group, the 8-methyl-5-(4-nitrophenyl)-9H-1,3-dioxolo-4,5-h//2,3/benzodiazepine of the formula II is reacted with an acylating agent of the formula IX, wherein each of Y and X' represents, independently, a leaving group, p is as stated above, and the obtained acylated compound of the formula VIII

-115-

B1
Cont

wherein X' and p are as defined above, is reacted with an amine of the formula HNR^7R^8 , wherein R^7 and R^8 are as stated above;

and, if desired, an obtained compound of the formula I, wherein R^2 represents a nitro group, R^1 , A and B are as defined in connection with the formula I, is transformed into a compound of the formula I, wherein R^2 stands for an amino group, by reduction;

and, if desired, an obtained compound of the formula I, wherein R^2 represents an amino group, R^1 , A and B are as defined in connection with the formula I, is reacted with a C_{1-4} alkanecarboxylic acid or a reactive acylating derivative thereof;

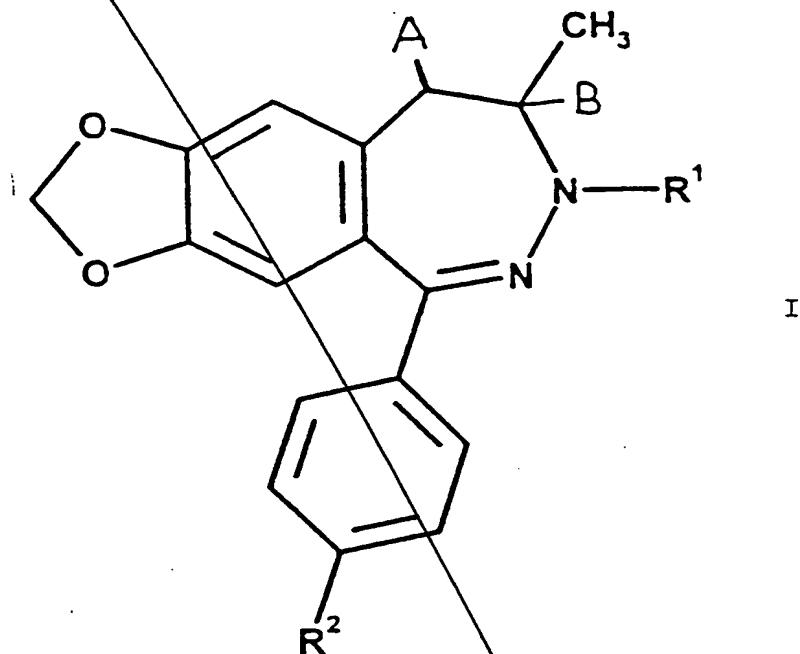
and, if desired, an obtained base of the formula I is converted to a pharmaceutically suitable acid addition salt or liberated from the acid addition salt.

-116-

9. A pharmaceutical composition comprising
 a 1,3-dioxolo/4,5-h//2,3/benzodiazepine
 derivative of the formula I

B1
Cont

CONTENTS OF DRAWINGS



wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R¹ stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group

or a group of the formula $-NR^3R^4$, wherein

R³ and R⁴ mean, independently, a hydrogen atom, a C₃₋₆ cycloalkyl group, a

C₁₋₄ alkoxy group, an amino group,

a phenyl group optionally substituted by one or two C₁₋₄ alkyl group(s),

a C₁₋₄ alkyl group which latter is

-117-

*B1
cont*

optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group, n has a value of 0, 1 or 2, m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula $-CO-(CH_2)_p-R^6$, wherein R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

0945541-054000

B1
cont

-118-

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cyclo-alkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group which latter is optionally substituted, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is

09435441.054000

-119-

31
cont

optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C₁₋₄ alkoxy group, and, in case of the phenoxy(C₁₋₄ alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,
R² stands for a nitro group, an amino group or a (C₁₋₄ alkanoyl)amino group, or a pharmaceutically suitable acid addition salt thereof as the active ingredient and one or more conventional carrier(s).

10. A pharmaceutical composition as claimed in Claim 9 comprising a 1,3-dioxolo-4,5-h//2,3/benzodiazepine derivative of the formula I, wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R¹ stands for a group of the formula

-(CH₂)_n-CO-(CH₂)_m-R, wherein

R represents a chloro atom, a pyridyl group or a group of the formula -NR³R⁴,

wherein

R³ and R⁴ mean, independently, a hydrogen atom, a cyclopropyl group, a C₁₋₄ alkoxy group, an amino group, a phenyl group optionally substituted by one or two methyl group(s) or a C₁₋₄ alkyl group which latter is optionally substituted by a phenyl group or a saturated

095005441-0540000

-120-

heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and the heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 methoxy groups,

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 methoxy groups, n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2.

R^2 stands for a nitro group or an amino group, or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

11. A pharmaceutical composition as claimed in Claim 10 comprising a 1,3-dioxolo-4,5-h//2,3/benzodiazepine derivative of the formula I, wherein

R^3 and R^4 represent, independently, a hydrogen atom, a cyclopropyl group, a methoxy group, an amino group, a dimethylaminophenyl group or a C_{1-2} alkyl group which latter is substituted by a phenyl, morpholino or piperazinyl group, wherein the piperazinyl group is substituted by a methoxyphenyl

-121-

B1
cont

group, or
 R^3 and R^4 form, together with the adjacent nitrogen atom and optionally a further nitrogen atom or oxygen atom, an imidazolyl, morpholino or piperazinyl group, wherein the piperazinyl group is substituted by a methoxyphenyl group,
 n has a value of 0 or 1,
 m has a value of 0 or 1,
 R^2 stands for a nitro group or an amino group,
A represents a hydrogen atom,
B means a hydrogen atom,
or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

12. A pharmaceutical composition as claimed in Claim 11 comprising a 1,3-dioxolo- $/4,5-h//2,3/benzodiazepine$ derivative of the formula I, wherein
 R^3 represents a hydrogen atom,
 R^4 stands for a cyclopropyl group, a methoxy group or an amino group,
 n has a value of 0,
 m has a value of 0,
 R^2 means an amino group,
A represents a hydrogen atom,
B means a hydrogen atom,
or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

13. A pharmaceutical composition as claimed in Claim 9 comprising an 8-methyl- $-7H-1,3-dioxolo/4,5-h//2,3/benzodiazepine$ derivative of the formula I, wherein

09435441 - 051000

-122-

~~A forms together with B a valence bond between the carbon atoms in positions 8 and 9,~~

~~R¹ represents a group of the formula -CO-(CH₂)₂-P-R⁶, wherein~~

~~R⁶ stands for a halo atom, a phenoxy group, a C₁₋₄ alkoxy group or a group of the formula -NR⁷R⁸, wherein~~

~~R⁷ and R⁸ mean, independently, a hydrogen atom, a guanyl group or a C₁₋₄ alkyl group which latter is optionally substituted by a phenyl group or a morpholino group, wherein the phenyl group is optionally substituted by one or two C₁₋₂ alkoxy group(s), or~~

~~R⁷ and R⁸ form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group or a saturated heterocyclic group having 5 or 6 members and comprising one or two nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 2 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C₁₋₄ alkyl) group or a phenoxy(C₁₋₄ alkyl) group, wherein in case of the substituents listed~~

SEARCHED - DECODED

*B1
Cont*

-123-

S'
cont

the phenyl or phenoxy group is optionally substituted by a halo atom or a C₁₋₄ alkoxy group,

p has a value of 0, 1 or 2,

R² stands for a nitro group or an amino group, or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

14. A pharmaceutical composition as claimed in Claim 13 comprising an 8-methyl-7H-1,3-dioxolo[4,5-h]2,3/benzodiazepine derivative of the formula I, wherein A forms together with B a valence bond between the carbon atoms in positions 8 and 9,

R² represents a nitro group or an amino group,

R¹ stands for a group of the formula

-CO-(CH₂)_p-R⁶, wherein

R⁶ means a chloro atom, a phenoxy group, or a group of the formula -NR⁷R⁸, wherein

R⁷ and R⁸ represent, independently,

a hydrogen atom, a guanyl group or a C₁₋₃ alkyl group optionally substituted by a phenyl group, a dimethoxyphenyl group or a morpholino group, or

R⁷ and R⁸ form with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group or a saturated heterocyclic group having 5 or 6 members and comprising one or two nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom,

CONFIDENTIAL DOCUMENT

-124-

B
cont

and said heterocyclic group is optionally substituted by one or two identical or different substituent(s) selected from the group consisting of a hydroxy group, a methoxyphenyl group, a fluorophenyl group, a benzyl group or a (methoxyphenoxy)-(hydroxypropyl) group,

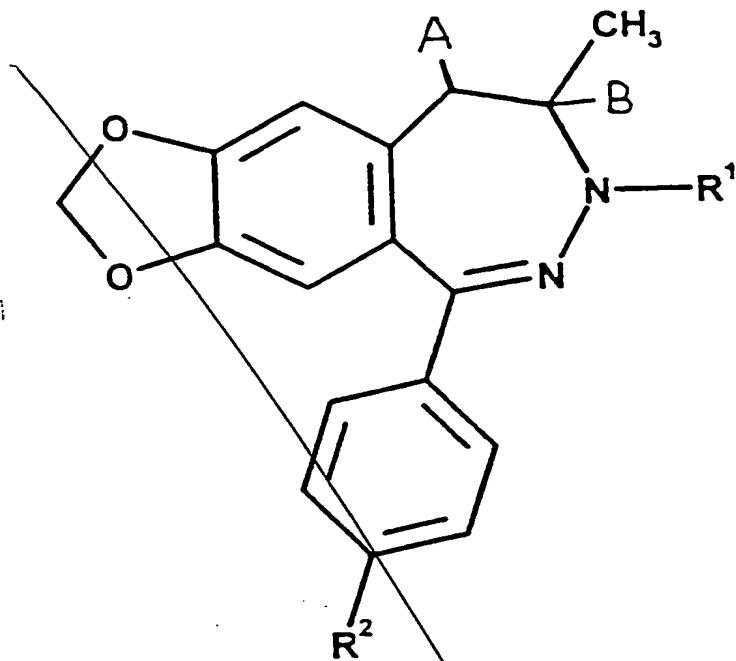
p has a value of 0, 1 or 2, or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

15. A pharmaceutical composition as claimed in Claim 14 comprising an 8-methyl-
-7H-1,3-dioxolo[4,5-h]2,3/benzodiazepine derivative of the formula I, wherein R² represents an amino group, R¹, A and B are as defined in Claim 6, or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

16. A method of treatment in which a patient suffering especially from epilepsy or a neurodegenerative disease or being in a state after stroke is treated with a non-toxic dose of a 1,3-dioxolo[4,5-h]2,3/benzodiazepine derivative of the formula I

SEARCHED - DECEMBER 2000

-125-

B' Cont

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R¹ stands for a group of the formula $-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein R³ and R⁴ mean, independently, a hydrogen atom, a C₃₋₆ cycloalkyl group, a C₁₋₄ alkoxy group, an amino group, a phenyl group optionally substituted by one or two C₁₋₄ alkyl group(s), a C₁₋₄ alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and

-126-

cont

comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group, n has a value of 0, 1 or 2, m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula $-CO-(CH_2)_p-R^6$, wherein R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group

SEARCHED - DECEMBER 1998

-127-

B1
Cont

which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group which latter is optionally substituted, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo

CONFIDENTIAL - SECURITY

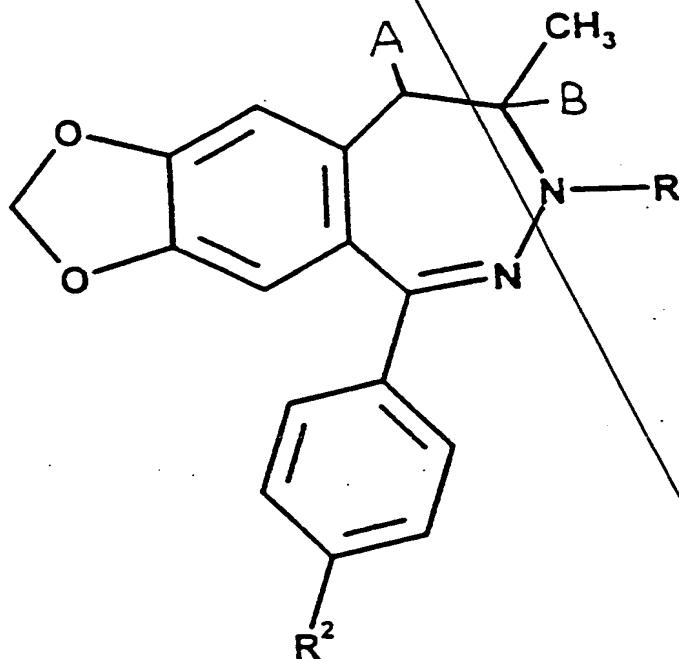
-128-

B/
cont

atom or a C_{1-4} alkoxy group, and, in case of the phenoxy(C_{1-4} alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,
 R^2 stands for a nitro group, an amino group or a (C_{1-4} alkanoyl)amino group, or a pharmaceutically suitable acid addition salt thereof.

17. A process for preparing a pharmaceutical composition suitable for the treatment of especially epilepsy, a neuro-degenerative disease or a state after stroke, characterized in that a 1,3-dioxolo/4,5-h/-/2,3/benzodiazepine derivative of the formula I



-129-

81
cont

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two C_{1-4} alkyl group(s), a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4}

alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that

05434411 - 062000

-130-

B1
cont

is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group, n has a value of 0, 1 or 2, m has a value of 0, 1 or 2, or A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case R^1 represents a group of the formula $-CO-(CH_2)_p-R^6$ wherein R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or R^7 and R^8 form together with the adjacent nitrogen atom an oxopyrrolidinyl group, a phthalimido group which latter is optionally substituted, or a saturated heterocyclic group

-131-

B1
cont

having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C₁₋₄ alkyl) group or a phenoxy(C₁₋₄ alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C₁₋₄ alkoxy group, and, in case of the phenoxy(C₁₋₄ alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,
*R*² stands for a nitro group, an amino group or a (C₁₋₄ alkanoyl)amino group, or a pharmaceutically suitable acid addition salt thereof, together with one or more conventional carrier(s), is converted to a pharmaceutical composition.

ms
B2
add
FS